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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/573,191	09/11/2007	Yusuke Sakai	8002P001	4940

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EXAMINER	
HOLLOMAN, NANNETTE	

ART UNIT	PAPER NUMBER
1612	

MAIL DATE	DELIVERY MODE
03/30/2011	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/573,191	SAKAI ET AL.	
	Examiner	Art Unit	
	NANNETTE HOLLOMAN	1612	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 January 2011*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-6 and 8-12* is/are pending in the application.

4a) Of the above claim(s) *11 and 12* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-6 and 8-10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *01/31/2011*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This Office Action is in response to the Request for Continued Examination filed on January 31, 2011. Applicants' arguments, filed January 31, 2011, have been fully considered. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

Claim Rejections - 35 USC § 103

(Previous Rejection)

Claims 3, 5 and 10 were rejected under 35 U.S.C. 103(a) as being unpatentable over Bowman et al. (US Patent No. 5,767,153) and further in view of Hellberg et al. (US Patent No. 6,342,524). This rejection is maintained and further applied to claims 1, 4, 6, 8 and 9.

Applicant's Arguments

Applicant argues Bowman does not disclose a prostaglandin $F_{2\alpha}$ derivative ($PGF_{2\alpha}$ derivative) of instant claim 1 and the bioavailability as disclosed in Bowman does not relate to the degradation of the drugs in the instant preparation. Applicant

argues Hellberg does not mention any addition of oil such as MCT in the preparation, nor does it disclose concrete components of an emulsion. Applicant further argues the Schneider reference, which was used for evidence, discloses when polysorbate 80 is employed as a surfactant, a concentration of PG decreases to 10% of the initial concentration after 30 days of storage at 55℃. However, when polyoxyethylated castor oil is added to the composition, the concentration of PG is at 50% of the initial concentration after 30 days of storage at 55℃. Wherein the compositions disclosed by the application, for example, formulation of 5 and 6, by contrast maintain almost 100% of the initial PG concentration relative to the initial concentration even after 4 weeks at 60℃, which is a more severe condition for storage than the above cases of Schneider. Such a special effect of the described and claimed composition could not be expected by one of skill in that prior to Applicant's invention. Applicant further argues a person of skill in the art would expect the unexpected results of the emulsion of latanoprost to also be expected for the prostaglandin esters recited in pending claim 1. Applicant's arguments filed have been fully considered but they are not persuasive.

Examiner's Response

In regard to claims 1, 4, 6, 8 and 9, as previously asserted in the Office action filed October 5, 2009, Bowman et al. disclose an ophthalmic emulsion composition, which may be administered to the eye in drop form (instant claims 8 and 9) (Abstract). Bowman et al. disclose the composition comprises oil, i.e. vegetable and medium chain triglycerides (instant claim 6) (column 2, lines 58-61); a water soluble polymer, i.e.

polyvinyl pyrrolidone (instant claim 4) (column 4, lines 7 and 8); water and a prostaglandin $F_{2\alpha}$ derivative; which reduce intraocular pressure (column 1, lines 10-13 and column 5, TABLE 1). The reference differs from claim 1 insofar as it is does not disclose the claimed prostaglandin. This deficiency is cured by Hellberg et al. Hellberg et al. was used to show the preferred $PGF_{2\alpha}$ derivative for treatment of glaucoma and ocular hypertension is latanoprost (Abstract and column 7, lines 54 and 55) and said composition may be in the form of an emulsion containing viscosity building agents, i.e. polyvinyl alcohol (column 9, line 1). Therefore, based on the teachings supra, generally, it is *prima facie* obvious to combine two compositions, each of which is taught by the prior art to be useful for same purpose, in order to form a third composition to be used for the very same purpose. The idea for combining them flows logically from their having been individually taught in the prior art. See MPEP 2144.06. Therefore, it would have been obvious to have combined latanoprost with the derivative of Bowman et al. since they are both known to treat glaucoma and the pressure associated with glaucoma.

Further, Applicant appears to be arguing the references individually. One cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). It is acknowledged that Bowman does not anticipate the instant claims. Hellberg et al. cures the deficiencies of Bowman to arrive at the instantly claimed invention as stated above by disclosing known $PGF_{2\alpha}$ derivatives for use in the types of compositions disclosed by Bowman. The invention of the instant claims is obvious in view of the combination of the

combined teachings and not the individual references. Therefore the reference cannot be argued individually.

The evidentiary reference Schneider was used to show that prostaglandins have low water solubility and are generally unstable; however, the stability can be increased with polyethoxylated castor oil. Furthermore, the stabilizing effect of the polyethoxylated castor oil increases with increasing the concentration of the oil, which is shown in FIG. 1 (Abstract, column 6 lines 16-22). The stability is shown in FIG. 1. It is seen that when polyoxyethylated castor oil is added to the composition, the concentration of PG is about 90% of the initial concentration after about 4 weeks of storage at 65°C.

Applicant's alleged unexpected results wherein it was recognized that an oil-in-water emulsion formulating latanoprost together with a medium chain fatty acid triglyceride and water-soluble polymer suppressed the degradation of latanoprost, do not appear to be unexpected. Specifically since it was shown by Schneider that oils increase the stability of prostaglandins and the concentration of the oil is a "result effective" variable, i.e. increasing the concentration increases the stability. As discussed above, the stability shown in FIG. 1, when polyoxyethylated castor oil is added to the composition, the concentration of PG is about 90% of the initial concentration after about 4 weeks of storage at 65°C, thereby showing the increase in stability. Therefore, one of ordinary skill in the art would reasonably expect the oil-in-water emulsion of Bowman in view of Hellberg, which comprises oil, i.e. medium chain triglyceride, would have an increased stability of the prostaglandin. Furthermore, the comparison does not appear to be proper, since the closest prior art, Bowman,

discloses an oil-in-water emulsion comprising a prostaglandin, while Applicant has compared and emulsion to a water based vehicle (Xalatan).

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to NANNETTE HOLLOMAN whose telephone number is (571)270-5231. The examiner can normally be reached on Mon-Fri 8:00am-5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Frederick Krass can be reached on 571-272-0580. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/N. H./
Examiner, Art Unit 1612

/Frederick Krass/
Supervisory Patent Examiner, Art Unit 1612